

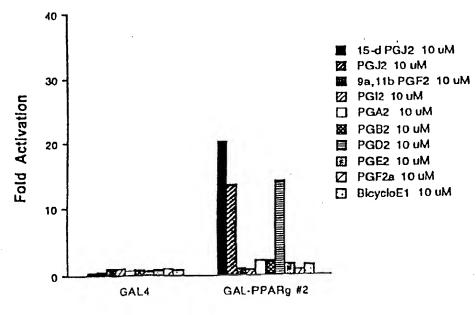
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(54) Title: SELECTIVE MODULATORS OF PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR-GAMMA, AND METHODS FOR THE USE THEREOF



(57) Abstract

In accordance with the present invention, there are provided a class of compounds which are capable of selectively modulating processes mediated by peroxisome proliferator activated receptor-gamma (PPAR- γ). The identification of such compounds makes possible the selective intervention in PPAR- γ mediated pathways, without exerting inadvertent effects on pathways mediated by other PPAR isoforms.

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INTERNATIONAL SEARCH REPORT

International Application No

| | | | r. /US 90/ | 05465 |
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| A. CLASS IPC 6 | SIFICATION OF SUBJECT MATTER A61K31/557 | | | |
| According | to International Patent Classification (IPC) or to both national clas | sification and IPC | | |
| B. FIELD | S SEARCHED | | | |
| Minimum of IPC 6 | documentation searched (classification system followed by classific A61K | ation symbols) | | |
| Documenta | tion searched other than minimum documentation to the extent tha | it such documents are inclu | ded in the fields sea | rched |
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| C. DOCUM | MENTS CONSIDERED TO BE RELEVANT | | | |
| Category * | Citation of document, with indication, where appropriate, of the | relevant passages | | Relevant to claim No. |
| х | PROCEEDINGS OF THE NATIONAL ACAD SCIENCES OF USA, | | · | 22,23 |
| | vol. 91, July 1994, WASHINGTON pages 7355-7359, XP002007699 S.A. KLIEWER ET AL.: "Different expression and activation of a f murine peroxisome proliferator-a receptors" | amily of | | |
| A | see the whole document GENE EXPRESSION, vol. 4, 1995, | | | 1-23 |
| | pages 281-299, XP000057446 M.E. GREENE ET AL.: "Isolation human peroxisome proliferator ac receptor gamma cDNA" | | | |
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| X Furt | her documents are listed in the continuation of box C. | Patent family me | embers are listed in | annex. |
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| 12 | . December 1996 | 18.12.9 | 96 | |
| Name and n | nailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 | Authorized officer | | |
| | NL - 2280 HV Rijswijk Tel. (+ 31.70) 340-2040, Tx. 31 651 epo nl, Fax: (+ 31-70) 340-3016 | De Jong, | В | |

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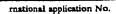




INTERNATIONAL SEARCH REPORT

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| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | | | | | |
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. | | | | |
| K,P | JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 22, 2 June 1995, MD US, pages 12953-12956, XP002007698 J.M.LEHMANN ET AL.: "An antidiabetic thiazolidinone is a high affinity ligand for peroxisome prolifirator-activated receptor" see the whole document | 22,23 | | | | |
| P,X | J. BIOL. CHEM., vol. 270, no. 41, 13 October 1995, pages 23975-23983, XP002008288 K. YU ET AL.: "Differential activation of peroxisome proliferator-activated receptors by eicosanoids" see the whole document | 1-23 | | | | |
| P , X | CELL, vol. 83, 1 December 1995, pages 813-819, XP000575884 S.A. KLIEWER ET AL.: "A prostaglandin J2 metabolite binds peroxisome proliferator-activated receptor gamma and promotes adipocyte differentation" see the whole document | 1-23 | | | | |
| P,X | CELL, vol. 83, 1 December 1995, pages 803-812, XP000575803 B.M. FORMAN ET AL.: "15-DEOXY-DELTA12,14-PROSTAGLANDING J2 IS A LIGAND FOR THE ADIPOCYTE DETERMINATION FACTOR PPAR GAMMA" see the whole document | 1-23 | | | | |



PCT/US 96/05465

INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Although claims 1-15, 22 and 23 are directed to a method of treatment of (diagnostic method practised on) the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet) This International Searching Authority found multiple inventions in this international application, as follows: As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: The additional search fees were accompanied by the applicant's protest. Remark on Protest No protest accompanied the payment of additional search fees.